

Editorials

Seminars in Health Care Delivery

AT A RECENT Annual Meeting of the Editorial Board it was suggested that in view of the growing importance of socioeconomics in the delivery of health care, the journal should begin to offer more on this subject for the information and perusal of its more than 54,000 readers. In response to this suggestion a series of Seminars in Health Care Delivery was planned.

The editors were fortunate indeed when Steven A. Schroeder, MD, agreed to be the editor for this series. Dr Schroeder not only is a distinguished clinician, a leading teacher of primary care internal medicine and consultant to a number of private foundations and government agencies, but he also is widely known for his scholarship and publications in many aspects of health care delivery. Among his many responsibilities, he currently serves as a member of the US Prospective Payment Assessment Commission and chairman of its Data Development Committee.

The journal welcomes Dr Schroeder and looks forward to the series of Seminars in Health Care Delivery that is being developed under his leadership, the first of which appears in this issue.

MSMW

New Roles for Activated Charcoal

DERLET AND ALBERTSON in their excellent review entitled "Activated Charcoal—Past, Present and Future" in this edition of the journal have provided a scholarly summary of the development, current uses and new roles of oral activated charcoal in the treatment of poisoned patients. They not only focus on the use of activated charcoal as an adsorbent of many common poisons and drugs to prevent their absorption from the gut but also review the role of multiple doses of oral charcoal in increasing the clearance of certain substances from the body (gastrointestinal dialysis).

As pointed out by the authors, a new form of superactivated charcoal is available and has been recently released for clinical use in the United States.¹ This charcoal (Super-Char) has a surface area of 2,500 to 3,500 m² per gram, or approximately three times as much as the older forms of activated charcoal.¹ This substance, as expected, is approximately three times as effective (on a weight basis) in both adsorbing drugs and in increasing the clearance of drugs from the body. The advantage of superactivated charcoal is that only approximately a third the amount of standard charcoal is necessary to decrease absorption or increase clearance of intoxicants comparably. There are some patients who are unable to drink 60 grams of charcoal but who can drink 20 grams. Thus, superactivated charcoal is an important advance in charcoal preparations and its use has been adopted in many institutions in the United States.

Activated charcoal use is not without limitations. Many drugs and intoxicants are not well adsorbed by activated charcoal, as pointed out by Derlet and Albertson. These include lithium, methanol and ethylene glycol. Moreover, there are

other drugs that, although they are adsorbed by activated charcoal, their clearance is not accelerated by multiple doses of oral charcoal.¹ For example, in one carefully done study with intravenously given imipramine hydrochloride (a tricyclic antidepressant), the imipramine clearance in subjects receiving multiple doses of activated charcoal was no greater than in those who received no charcoal.² Similarly, digoxin clearance is only increased by approximately 30% with multiple doses of oral activated charcoal in normal subjects.¹ It is experimentally clear, however, that many drugs, including salicylates, barbiturates, carbamazepine, dapsone, digitoxin, nadolol, theophylline and the pesticide chlordecone, have greatly increased clearances by multiple doses of oral activated charcoal.¹

In previous publications, we have proposed a simple pharmacokinetic model to explain the ability or lack of ability of multiple doses of activated charcoal to increase the clearance of drugs and poisons from the body.^{1,3} The total body clearance (Cl_T) of a drug or poison is the summation of clearances by all methods of removal from the body. Thus,

$$Cl_T = Cl_K + Cl_L + Cl_{GI},$$

where the subscripts K, L and GI refer to elimination by the kidney, metabolism and excretion by the liver and removal by charcoal through the gastrointestinal tract, respectively. Therefore, the significance of the contribution of charcoal on Cl_{GI} to Cl_T will depend on the magnitudes of Cl_{GI} relative to Cl_K and Cl_L. We have shown this by comparing the effect of charcoal on the clearance of theophylline as a model drug in normal subjects and patients with hepatic cirrhosis. As the endogenous theophylline clearance (Cl_L and Cl_K, due to hepatic and renal elimination) decreased in normal subjects and in patients with hepatic dysfunction, the effect of charcoal (Cl_{GI}) on theophylline clearance (Cl_T) increased.^{1,3} Therefore, even if endogenous clearance declines to zero, the total clearance (Cl_T) will never be less than the Cl_{GI} achieved by charcoal in the gut.

The rate of removal of a drug or poison by charcoal in the gut is strongly influenced by the apparent volume of distribution (V) of the drug or poison.¹

$$\begin{aligned} \text{Rate of removal by charcoal} &= Cl_{GI} \times C \\ &= Cl_{GI} \times A/V, \end{aligned}$$

where C is the concentration of drug or poison in the plasma and A is the amount of drug or poison in the body. Therefore, for any given amount of drug or poison (A) and clearance rate (Cl_{GI}), the rate of removal by charcoal in the gut is inversely related to the volume of distribution. That is, drugs with large volumes of distribution will not be effectively removed by oral activated charcoal. An example of such a drug is imipramine.

We can make some general predictions as to which drugs and poisons may or may not be effectively removed from the body by multiple doses of oral activated charcoal.¹ It would be expected that drugs or poisons that can easily diffuse across the gut membrane and have small volumes of distribution (less than 1 liter per kilogram of body weight) would be effectively